## REMARKS

Status of the Claims

Claims 1-4, 6-19 and 28-30 are pending in the present application, new Claims 29 and 30 having been added in the present amendment, Claim 5 having been canceled in the present amendment, and Claims 20-27 having been canceled previously as being directed to a non-elected invention. Claims 1, 2, 4, 6, 9, 15, and 28 have been amended to more clearly define the invention.

Claims Rejected under 35 U.S.C § 112, Second Paragraph

The Examiner has rejected Claims 1-19 under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserts that the phrase relating to *a reactor being configured to operate continuously over a period of time* is not clear, because the claim does not define what structural elements of the reactor provide such functionality.

Applicants have amended independent Claims 1 and 15; thereby obviating the indefiniteness rejection. Essentially, the structure in the amended claims that provides such functionality is a controller programmed to provide the recited functionality. It should be noted that by amending the independent claims, the rejection of the dependent claims is also obviated. Accordingly, the rejection of Claims 1-19 under 35 U.S.C § 112, second paragraph, should be withdrawn.

The Examiner has rejected Claim 28 under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserts that the recitation of *controlling said reaction module to automatically produce the desired chemical product from the first reactant* is unclear because the claim does not define what elements of the reaction module are controlled.

Applicants have amended Claim 28; thereby obviating the indefiniteness rejection. Essentially, the phrase objected to by the Examiner has been deleted. In some embodiments, the reaction module includes a heat exchanger that can be controlled by the system controller. Because Claim 28 does not recite a heat exchanger, the system controller need not be controllably coupled to the reaction module. Accordingly, the rejection of Claim 28 under 35 U.S.C § 112, second paragraph, should be withdrawn.

Claims Rejected under 35 U.S.C § 103

The Examiner has rejected Claims 1-6, 9, 11-16, and 18 under 35 U.S.C § 103(a) as being obvious over Rosenberg (WO0009300625). The Examiner admits that Rosenberg does not teach each



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element recited in applicants' claims, but asserts that it would have been obvious to one of ordinary skill in the art to modify Rosenberg's apparatus to achieve an equivalent invention. Applicants respectfully disagree for the following reasons.

Applicants have amended Claim 1 to further define the system controller as being programmed to "*continuously operate the automated sequential reactant system over a period of time, during which the system controller implements the steps of:*

*(i) controlling the first automated reactant supply and the first supply valve to introduce a reactant required to produce a first desired product into the general purpose reactor for a period of time sufficient to produce a desired quantity of the first desired product;*

*(ii) controlling the solvent supply to flush the general purpose reactor with the solvent after the desired quantity of the first desired product has been produced; and*

*(iii) repeating steps (i) and (ii) with different reactants as necessary to produce each other desired chemical product needed to complete the substance library, such that a volume of solvent separates each different desired product discharged from the general purpose reactor, thereby achieving discharge of a continuous flow of fluid from the general purpose reactor during the period of time the automated sequential reaction system is operated continuously, the continuous flow comprising different desired products separated by a volume of the solvent.* Independent Claim 15 has been amended in a substantially similar fashion.

Applicants' FIGURE 4 clearly shows a continuous flow including a plurality of different products separated by a volume of solvent. The system disclosed by Rosenberg is specifically configured to operate so that a flow of a fluid ***is not*** continuously discharged from the reaction chamber while the system is being operated. Instead, the outflow of fluid from the reaction chamber is cyclically interrupted each time the syringe pump changes position. This aspect of Rosenberg's system is clearly described in connection with Rosenberg's FIG. 4 and the related text on page 24, line 1, to page 25, line 4. Essentially, Rosenberg's system is based on having a syringe pump (MSP) disposed downstream of the reaction chamber (RC). In the I-position, the syringe pump sucks a fluid (either a solvent, a deblocking agent, or an amino acid, depending on which portion of the reaction cycle is being implemented) from the corresponding fluid supply, through the reaction chamber, and into the syringe pump. The syringe pump is then switched to the O-position, so that any fluid in the syringe pump is discharged to either a waste collection vessel (solvent) or a recycling flask (amino acid). This process is repeated until each required



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fluid is introduced into the reaction chamber. Significantly, fluid is only discharged from the reaction chamber when the syringe pump is in the I-position. Whenever the syringe pump is in the O-position, the fluid line coupling the reaction chamber to the syringe pump is blocked, and thus no fluid can exit the reaction chamber. The Examiner is correct that Rosenberg's operates continuously, in that different fluids are introduced and removed from the reaction chamber continuously until a desired product has been produced. However, it must be recognized that in the Rosenberg system, fluid is discharged from the reaction chamber ***cyclically***, not continuously.

Furthermore, the liquid being discharged from the reaction chamber is a function of the cycle. In some cycles, the fluid being discharged from the reaction chamber is a solvent. In other cycles, the fluid being discharged from the reaction chamber is an amino acid (used for coupling reactions). Significantly, the amino acid being discharged is not the desired product, rather the amino acid is simply a reagent that has been introduced into the reaction chamber to add additional sequences to an oligomer bound to a support held within the reaction chamber. In applicants' system, either the solvent or a product is discharged from the reactor. In Rosenberg's system, solvents and reagents are cyclically discharged from the reactor. It appears that each embodiment disclosed by Rosenberg operates in the same fashion, i.e., that the output from the reaction chamber is cyclically interrupted, and that the output from the reactor comprises solvents and reagents in various cycles. There is no evidence to conclude that it would have been obvious to one of ordinary skill in the art at the time of the invention to modify Rosenberg system such that a fluid flow discharges continuously from the reactor while the system is operational, where the continuous fluid comprises different chemical products separated by a volume of solvent. Significantly, there is no evidence that an artisan of ordinary skill would have recognized any benefit that could be achieved by making such a substitution, nor is it evident that such a substitution would solve any problem that had been recognized by the art.

In the Examiner's *Response to Arguments*, the Examiner notes that Rosenberg specifically discloses that reactants and solvents are passed through the reaction chamber continuously, rather than being discharged after each pass. It is important to recognize that such language does not mean that a fluid continuously flows out of the reaction chamber. Rather, this language is directed to the concept that amino acid solutions are introduced into the reaction chamber, then withdrawn from the reaction chamber and directed into a recycling flask, and then drawn back into the reaction chamber once again (that is, the amino acid solutions are not discarded after passing through the reaction chamber only once). The amino



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acid solution may be recycled through the reaction chamber many different times. However, the amino acid solution does not flow continuously out of the reactor (i.e., fluids do not continuously flow out of the reactor without interruption). When the syringe pump is in the O-position and being used to push the amino acid solution into the recycling flask, no fluid can flow out of the reactor. The only time the fluid can flow out of the reactor is when syringe pump is in the I-position. Each time the syringe pump switches between the I-position and the O-position, fluid flow out of the reaction chamber is interrupted. Applicants have amended independent Claims 1 and 15 to clearly recite that the system controller is configured to operate the reactor so that a fluid flow (of either product or solvent) is continuously discharged from the reactor.

In the Examiner's *Response to Arguments*, the Examiner additionally notes that reactors for continuous catalytic processes that may include solid supports are well-known. Regardless of whether such an assertion is correct, the solid support disclosed by Rosenberg is clearly intended to provide a substrate upon which oligmers can be generated by cyclically passing different reagents through the reaction chamber. Such a synthesis, as disclosed by Rosenberg, requires cycling reagents and solvents through the reaction chamber, such that fluid flow out of the reaction chamber is cyclically interrupted. There is no evidence that it would have been obvious to one of ordinary skill in the art to modify Rosenberg' synthesis so that a flow of fluid is continuously discharged from the reaction chamber while the system is being operated.

Independent Claims 1 and 15 distinguish over the cited art because the system controllers recited in each independent claim control the processing systems to achieve a continuous flow of fluid out of the reactor, and the continuous flow comprises different products separated by a volume of solvent. It is well recognized that dependent claims are patentable for at least the same reasons as the claims upon which they depend. Accordingly, the rejection of Claims 1-6, 9, 11-16, and 18 under 35 U.S.C § 103(a) as being obvious over Rosenberg, should be withdrawn.

Furthermore, the language of Claim 15 specifically recites the controller as manipulating the flow rates of the reactants to accommodate different reaction times for different reactions, the controller establishing a relatively higher flow rate for reactions requiring a relatively shorter reaction time, and the controller establishing a relatively slower flow rate for reactions requiring a relatively longer reaction time. Such a controller is not disclosed or suggested by Rosenberg. Significantly, Rosenberg teaches that slower reactions are facilitated by increasing the number of times an amino acid solution is cycled



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through the reaction chamber, but ***not*** by manipulating a flow rate of the reactants. Claims 15, 16, and 18 further distinguish over the cited art for this additional reason.

Referring to Claims 6 and 18, the Examiner has admitted that Rosenberg does not specifically teach a detector located between the reaction chamber and the output valve. The Examiner has asserted that the incorporation of such a detector would have been obvious to one of ordinary skill in the art in order to control the process of product formation. Applicants respectfully disagree.

Applicants do not understand the basis for this rejection, in light of the Examiner's statement that Claim 28 would be allowable if rewritten to overcome the rejection under 35 U.S.C. § 112, because the prior art does not teach or fairly suggest *an automated sequential reaction system comprising an automated detector disposed between a reaction module and an output valve coupled to the system controller, the automated detector providing output signal to the system controller that is indicative of whether a spent solvent or a desired chemical product is flowing from the reaction module, the system controller responding to the output signal to actuate the output valve to selectively couple the reaction module in fluid communication with the automated product collector (if the output signal indicates that a desired product is flowing from the reaction module), or to selectively couple the reaction module in fluid communication with the spent solvent reservoir (if the output signal indicates that a spent solvent is flowing from the reaction module).*

Both Claims 6 and 18 recite substantially the same concept. Claim 6 recites an automatic detector configured to provide *an output signal to the system controller that is indicative of whether a spent solvent or a desired chemical product is flowing from the reaction module, said system controller responding to the output signal to actuate the output valve to:*

*(a) selectively couple the reaction module in fluid communication with the automated product collector if the output signal indicates that a desired product is flowing from the reaction module; and*

*(b) selectively couple the reaction module in fluid communication with the spent solvent reservoir if the output signal indicates that a spent solvent is flowing from the reaction module.*

Claim 18 uses slightly different language, but parsing Claim 18 makes it clear that the detector must be capable of distinguishing a solvent from a product, so the system controller directs solvents to the spent solvent reservoir and products to the product collector.



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Because Claims 6 and 18 are so closely related to Claim 28, it is not apparent why Claim 28 is allowable, but Claims 6 and 18 are not. Clearly, Claims 6 and 18 distinguish over the cited art for substantially the same reason as Claim 28. Accordingly, the rejection of Claims 6 and 18 as being obvious over Rosenberg should be withdrawn.

Patentability of Newly Added Claims

Newly added Claim 29 recites the element added to Claims 1 and 15 to distinguish over the cited art. Essentially, Claim 29 recites an automated sequential reaction system for producing a plurality of different products, which incorporates a first reactant delivery structure, a solvent delivery structure, a reactor, and a system controller, the system controller being:

*controllably connected to said first reactant delivery structure and said solvent delivery structure, the system controller being configured to continuously operate the automated sequential reactant system over a period of time, during which the system controller implements the steps of:*

*(i) controlling the first reactant delivery structure to introduce a reactant required to produce a first desired product into the reactor for a period of time sufficient to produce a desired quantity of the first desired product;*

*(ii) controlling the solvent delivery structure to flush the reactor with the solvent after the desired quantity of the first desired product has been produced; and*

*(iii) repeating steps (i) and (ii) for each additional reactant required to produce an additional desired product, such that a volume of solvent separates each different desired product discharged from the reactor to produce the substance library of different desired chemical products, thereby discharging a continuous flow of fluid from the reactor during the period of time the automated sequential reaction system is operated continuously, the continuous flow of fluid comprising different desired products separated by a volume of the solvent.*

As discussed in detail above, Rosenberg does not teach or suggest a system controller configured to achieve a continuous flow of fluid from a reactor, where the continuous flow of fluid comprises different products separated by a volume of solvent. It appears that modifying Rosenberg to achieve an equivalent controller would require an impermissible use of hindsight. Claim 29 therefore distinguishes over the cited art.



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Newly added Claim 30 recites a sequential reaction system including reactant supply, a reactor, a heat exchanger, and a system controller, the system controller being configured to continuously operate the system to produce a plurality of chemical products, by controlling the reactant supply and the heat exchanger. Significantly, Claims 7, 8, and 19 each relate to a sequential reaction system comprising a heat exchanger. The Examiner has not rejected Claims 7, 8, and 19 over the prior art, indicating that a continuously operating sequential reaction system comprising a heat exchanger distinguishes over the cited art. Claim 30 distinguishes over the cited art for substantially the same reasons as Claims 7, 8, and 19.

Accordingly, all of the claims now submitted define patentable subject matter that is neither anticipated nor obvious in view of the prior art cited. The Examiner is thus requested to issue the present patent in view of the amendments and the remarks submitted above. If there are any questions that might be addressed by a telephone interview, the Examiner is invited to telephone the undersigned attorney, at the number listed below.

Respectfully submitted,

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